REMARKS/ARGUMENTS

Claim Objection

The Examiner holds that claim 11 is a duplicate of claim 9. Applicant respectfully points out that the scope of claim 11 is different from the scope of claim 9. Claim 9 reads on [T]he process of claim 6 wherein the molar amount of acetic anhydride is more than 3 times the molar amount of DTPA; whereas claim 11 reads on [T]he process of claim 6 wherein the molar amount of acetic anhydride is about 3 times the molar amount of DTPA. Hence claims 9 and 11 are both considered to be allowable claims on the subject matter of the present invention. Applicant directs the Examiner's attention to page 4, lines 12 to 13 and to example 2 of the description where it is noted and demonstrated that a molar amount of acetic anhydride of about 3 times the molar amount of DTPA is particularly preferred.

Claim Rejections – 35 USC § 102

Claims 1, 6, 9-11, 13-15 and 17 stand rejected under 35 USC 102(b) as being anticipated by Gibby (US 4,822,594). Applicant has withdrawn claim 17 from consideration.

The Examiner alleges that Gibby in column 3, lines 52-61 of the specification teaches a process for the production of DTPA-bis(anhydride) by reacting DTPA with a molar amount of acetic acid four times that of DTPA and a molar amount of pyridine that is six times the amount of DTPA at a temperature from 45°C to about 85°C. Applicant has carefully studied the cited lines and notes that column 3, lines 52-61 teaches the preparation of a chelate-bisanhydride by reaction with e.g. acetic acid in an anhydrous base such as e.g. pyridine, but nowhere mentions molar amounts of the reactants as the Examiner asserts.

The Examiner further points to Example 1 in the Gibby patent and to the reaction temperature and reaction time therein. In this example, specific amounts of the reactants DTPA (80 grams), anhydrous pyridine (100 ml – corresponding to 98 grams) and anhydrous

acetic acid (76 ml – corresponding to 82 grams) are reacted to form DTPA bis-anhydride. As will be evident from the description of the present application, see page 1, lines 29 to 32 of the published international application WO 2005/058846; Applicant has calculated the molar amount of pyridine to be 6.2 times the molar amount of DTPA.

Gibby therefore does not teach the process as claimed in claims 1 to 16 wherein a molar amount of pyridine equal or less than 6 times the molar amount of DTPA is used. Applicant respectfully submits that claims 1 to 16 are novel over Gibby and respectfully submits that the objections to claims 1, 6, 9-11, 13-15 should be withdrawn.

Claims 1, 6, 10, 11, 13, 14 and 17 stand rejected under 35 USC 102(b) as being anticipated by deLearie et al (US 5,508,388). Applicant has withdrawn claim 17 from consideration.

With reference to examples 1 and 2 of deLearie at al., the Examiner notes that a process for the production of DTPA-bis(anhydride) by reacting DTPA with acetic acid and pyridine in the molar ratio of 1.0:3.0:4.5 respectively and under specified temperatures is described.

Applicant will draw the Examiner's attention to that in addition to the three reactants mentioned above, deLearie et al. also uses acetonitrile in the reaction. deLearie et al. aims to reduce the amount of pyridine in the preparation of the anhydride reaction, see col. 3, lines 23 to 27. However, deLearie et al. found that acetonitrile should also be used in the reaction. In example 2, the effect of temperature and acetonitrile addition was investigated, and it was concluded that DTPA bis-anhydride was best prepared between 55°C and 65°C with 0.5 ml acetonitrile per gram DTPA.

Applicant does not use acetonitrile in the reaction which is evident from claim 1 where DTPA, acetic anhydride and pyridine are the only reactants used. Applicant directs the Examiner's attention to the specification of the present application, see page 2, lines 8-28,

where it is stated that the addition of acetonitrile is not desirable and that one object of the present invention is to avoid the use of acetonitrile in the process.

deLearie et al. therefore does not teach all and every elements of the present invention. Applicant respectfully submits that the rejections for claims 1, 6, 10, 11, 13, 14 under 35 USC 102(b) should be withdrawn.

Claim Rejections – 35 USC § 103

Claims 1 to 17 stand rejected under 35 USC 103(a) as being unpatentable over Dazzi (US 3,660,388). Applicant has withdrawn claim 17 from consideration.

Applicant was aware of the technology described by Dazzi prior to the present invention and directs the Examiner's attention to page 1, lines 20 to 27 of the description in the present application (published international application WO 2005/058846). Dazzi uses 6.5 moles of pyridine per mole of DTPA as can be calculated from the amounts in grams in example 9, which applicant holds as the closest description of this prior art. The information provided in example 9 further specifies conditions of the description in col. 1, lines 67 to 71 (which applicant finds more relevant than lines 45 to 55 as cited by the examiner), and also col. 2, line 68 to col. 3, line 8 of the patent as cited by the Examiner and provides one skilled in the art with information on how to work the invention of Dazzi.

As discussed in the specification of the present application, it is known that pyridine is toxic and relatively expensive and that there has been a desire to reduce the amount of pyridine to a minimum, see page 2, lines 8 to 12 of the description (published international application WO 2005/058846). On the other side, it was also known, e.g. from Dazzi, that a tertiary nitrogen base or mixtures thereof, such as pyridine or alkylated pyridines, should be added to the reaction since it is said to have the advantage to accelerate the reaction and improve the yield (col. 3, lines 2 to 6).

Applicant surprisingly found that not only was it possible to reduce the amount of the toxic and expensive chemical pyridine, but the yield of DTPA-bis(anhydride) and the reaction rate could also be maintained at a surprisingly high level as demonstrated in examples 1 to 7 in the present application. This was wholly unexpected since the industry standard was to use about 10 molar amount of pyridine per mole of DTPA in industrial processing of DTPA bis(anhydride). No published art has indicated that it would be possible to reduce the amount of pyridine to be equal to or below the molar ration of 6 times the molar amount of DTPA or even further without the addition of other non-desirable chemicals such as e.g. acetonitrile. The present invention is not a mere discovery of optimum workable ranges by routine experimentation but represent a genuine step forward in this area of technology. Applicant therefore maintains that the present invention as claimed in claims 1 to 16 would not be obvious to one skilled in the art based on the teaching of Dazzi.

Claims 1 to 17 stand rejected under 35 USC 103(a) as being unpatentable over Wagner (US 4,698,263). Applicant has withdrawn claim 17 from consideration.

Applicant was aware of the technology described by Wagner prior to the present invention and points the Examiner's attention to the paragraph joining pages 1 and 2 of the description of the present application (published international application WO 2005/058846). Wagner uses 7.5 moles of pyridine per mole of DTPA, see col. 12, lines 1 to 18. The ratio 7.5 is calculated from the amount is DTPA (100mmole) and the amounts of pyridine (60 ml which corresponds to 59 grams).

As discussed in the published international application WO 2005/058846 of the present application, it is known that pyridine is toxic and relatively expensive and that there has been a desire to reduce the amount of pyridine to a minimum, see page 2, lines 8 to 27 of the description.

For the same arguments as used for Dazzi above, applicant holds that the present invention is not a mere discovery of optimum workable ranges by routine experimentation

but represent a genuine step forward in this area of technology. Applicant therefore maintains that the present invention as claimed in claims 1 to 16 would not be obvious to one skilled in the art based on the teaching of Wagner.

Claims 1 to 17 stand rejected under 35 USC 103(a) as being unpatentable over Gibby (US 4,822,594). Applicant has withdrawn claim 17 from consideration.

As will be apparent from page 1, lines 29 to 32 of the description of the present application (published international application WO 2005/058846), applicant was also aware of the technology described by Gibby prior to the present invention. Gibby uses 6.2 moles of pyridine per mole of DTPA, see the calculations presented above.

As discussed in the specification of the present application, at the time of this invention it was known that pyridine is toxic and relatively expensive and that there has been a desire to reduce the amount of pyridine to a minimum, see page 2, lines 8 to 27 of the description.

For the same arguments as used for Dazzi and Wagner above, applicant holds that the present invention is not a mere discovery of optimum workable ranges by routine experimentation but represent a genuine step forward in this area of technology. Applicant therefore maintains that the present invention as claimed in claims 1 to 16 would not be obvious to the man skilled in the art based in the teaching of Gibby.

Claims 1 to 17 stand rejected under 35 USC 103(a) as being unpatentable over deLearie et al. (US 5,508.388). Applicant has withdrawn claim 17 from consideration.

As will be apparent from page 2, lines 8 to 27 of the description of the present application (published international application WO 2005/058846), applicant was also aware of the technology described by deLearie et al. prior to the present invention. As explained above, deLearie et al. wished to reduce the amount of pyridine in the produ tion of DTPA-

bis(anhydride) for the same reasons as the applicant of the present invention, since pyridine is highly toxic and relatively expensive, see col. 3, lines 23 to 27 in the patent. It is also known that in the formation of DTPA-bis(anhydride) from DTPA and acetic acid anhydride, acetic acid produced must be neutralized with a base. Pyridine is considered as a preferred base since it results in a high purity final product, see col. 2, lines 56 to 66. Applicant cannot see that deLearie et al. in col. 2, lines 59-60 states anything about that [p]yridine is a particular active base that accelerates the reaction and improves the yield as the examiner states. The accelerating properties of pyridine are however discussed by Dazzi as noted above and in the description of the present application. It was well known from the prior art that the amount of pyridine added in this reaction influences the reaction speed and also the purity of the product.

While deLearie et al. reduced the amount of pyridine they also found that acetonitrile should be added as explained above. Applicant however wishes to reduce the amount of pyridine without the addition of further reactants and in particular to avoid the use of acetonitrile which is poisonous. Hence, applicant with the present invention surprisingly found that the amount of pyridine could be reduced to a molar amount of equal to or less than 6 times the molar amount of DTPA without addition of further reactants such as acetonitrile. The present invention therefore solves the reduction of addition of pyridine in an entirely different manner than do deLearie et al. deLeari et al. does nowhere indicate the solution reached to in the present invention. In reaching to a solution of the problem in an entirely different manner than do deLeari et al., the solution reached to in the present invention reaches far beyond the mere discovery of optimum or workable ranges by routine experimentation.

Applicant has in addition considered if the teachings in any combination of Dazzi and/or Wagner and/or Gibby and/or deLeari et al. could be held to render the present invention obvious. Since all these prior art citations reads on the reductions of pyridine to above the molar amount of 6 times the molar amount of DTPA or to include use of the additional reactant acetonitrile, applicant holds that none of the cited prior art in combination

would render the present invention obvious over the prior art. Applicant therefore respectfully submits that claims 1 to 16 fulfill the requirements to overcome 35 USC 103(a).

In view of the foregoing favorable reconsideration of the claim rejections under 35 USC § 103 is respectfully requested.

CONCLUSION

In view of the amendments and remarks herein, Applicant believes that each ground for objection or rejection made in the instant application has been successfully obviated or overcome, and that all the pending claims, 1-16, are in condition for allowance. Withdrawal of claim 17 and allowance of claims 1-16 of the current application is respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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